Test Plan For 2-Nitropropane

(CAS No. 79-46-9)

OVERVIEW

The Dow Chemical Company agrees to sponsor 2-nitropropane (CAS No. 79-46-9) in the U.S. EPA High Production Volume Chemical Program. The sponsor hereby submits a test plan for this substance. It is the sponsor's intent to use existing data, plus modeled data to fulfill the Screening Information Set (SIDS) endpoints.

Table 1. Test Plan Matrix for 2-nitropropane (CAS No. 79-46-9)

CAS No. 79-46-9	Information	OECD Study	Other	Estimation	GLP	Acceptable	New Testing Required
ENDPOINT	Y/N	Y/N/	Y/N	Y/N	Y/N	Y/N	Y/N
PHYS/CHEM PROPERTIES							
Melting Point	Y	N	Y	N	N	Y	N
Boiling Point	Y	N	Y	N	N	Y	N
Vapor Pressure	Y	N	Y	N	N	Y	N
Partition Coefficient	Y	N	Y	N	N	Y	N
Water Solubility	Y	N	Y	N	N	Y	N
ENVIRONMENTAL FATE							
Photodegradation	Y	N	Y	Y/N	N	Y	N
Stability in Water	Y	N	Y	N	N	Y	N
Biodegradation	Y	Y/N	Y	N	ND	Y	N
Transport between Environmental Compartments (Fugacity)	Y	N	Y	Y	N	Y	N
ECOTOXICITY							
Acute Toxicity to Fish	Y	Y/N	N	N	ND	Y	N
Acute Toxicity to Aquatic Invertebrates	Y	Y	N	N	ND	Y	N
Toxicity to Aquatic Plants	Y	Y	N	N	ND	Y	N
TOXICOLOGICAL DATA							
Acute Toxicity (Inhalation)	Y	N	Y	N	Y/N	Y	N
Repeated Dose Toxicity (NR)	Y	N	Y	N	N	Y	N
Genetic Toxicity-Mutation	Y	N	Y	N	N	Y	N
Genetic Toxicity-Chromosomal Aberrations	Y	N	Y	N	N	Y	N
Toxicity to Reproduction (NR)	Y	N,S	Y	N	N,S	N,S	N
Developmental Toxicity	Y	N,S	Y	N	ND,S	Y,S	N
Carcinogenicity (NR)	Y	N	Y	N	N	Y	N
OTHER TOXICITY DATA							
Skin Irritation (NR)	Y	N	Y	N	Y	Y	N
Eye Irritation (NR)	Y	N	Y	N	Y	Y	N
Sensitization (NR)	Y	N	Y	N	ND	Y	N
Epidemiology (NR)	Y	N	Y	N	N	Y	N

Y = yes; N = no; ND = no data; NR = not required; S = GLP surrogate study included in evaluation

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1. Introduction

The Dow Chemical Company has agreed to provide screening hazard information under the U.S. EPA High Production Volume Chemical Program for 2-nitropropane (CAS No. 79-46-9). This plan identifies and assesses data that will be used to fulfill screening information endpoints.

2. Designation of Test Substance

The test substance presented in this test plan is 2-nitropropane (CAS No. 79-46-9). The substance is a colorless liquid, with a molecular formula of $CH_3CH(NO_2)CH_3$

This substance has the following synonyms:

Propane, 2-nitro
Dimethylnitromethane
Isonitropropane
Nitroisopropane
B-Nitropropane
Sec-Nitropropane

Typical purity of the commercial material is ≥94%.

3. General Use and Exposure Information

The substance is primarily used within ANGUS Chemical manufacturing sites as a closed-system intermediate; however, a small amount is sold to a limited customer base. Exposure to 2-nitropropane is strictly limited due to its flammability and carcinogenic potential in experimental animals. Use information is summarized in Appendix I.

4. Criteria for Determining Adequacy of Data

All available studies were reviewed and assessed for adequacy according to the standards of Klimisch *et al.* (1997). Studies receiving a Klimisch rating of 1 or 2 were considered to be adequate.

5. Discussion of Available Test Information

The test plan matrix (as shown in Table 1 on page 2) was constructed after a careful evaluation of all existing data (see below). This matrix is arranged by study type (columns) and screening data endpoints (rows), and indicates if data are provided for each end point in the sets of robust summaries.

5.1 Chemical and Physical Properties

The results of chemical/physical property testing are shown in Table 2.

Table 2. Chemical/physical properties of 2-nitropropane (CAS No. 79-46-9)

Endpoint	Value
Molecular weight grams/mol	89.09
Melting point	-91.3 ºC
Boiling point	120.2 ºC
Relative density	0.988 g/cm^3
Vapor pressure	17.32 hPa @ 20 deg C
Partition coefficient (Log Pow or Kow)	-0.63
Water solubility	17.4 g/l

5.1.1 Melting Point

A melting point of -91.3 ºC is cited in a standard reference (Lide, 1995-1996).

5.1.2 Boiling Point

A boiling point of 120.2 ºC at 1013 hPa is cited in a standard reference (Lide, 1995-6).

5.1.3 Vapor Pressure

The vapor pressure of 2-nitropropane is 17.32 hPa at 20ºC according to a standard reference (Holcomb and Dorsey, 1949).

5.1.4 Octanol/Water Partition Coefficient

Log Pow was determined experimentally to be -0.63 according to an unpublished report (Lhotak, 1996).

5.1.5 Water Solubility

2-Nitropropane is highly soluble in water with a water solubility of 17.4 g/l, according to a standard reference source (Lide, 1995-1996).

5.1.6 Summary/Test Plan for Physical Properties

Adequate data are available from standard reference sources (or estimation in the case of partition coefficient) to characterize all physical property endpoints for 2-nitropropane. 2-Nitropropane is a water soluble liquid with appreciable vapor pressure. No new testing is needed.

5.2 Environmental Fate/Pathways

Results of environmental fate modeling and studies are summarized in Table 3.

Table 3. Environmental fate parameters for 2-nitropropane

Endpoint	Value
Direct Photolysis	67.8% after 24 hours
Indirect Photolysis (OH sensitizer) (Hydroxyl Radical Rate Constant)* (Atmospheric $T_{1/2}$)*	 1.7 E-13 cm^3/molecule-sec 63.6 days
Stability in Water	Stable to hydrolysis
Henry's Law Constant*	1.25 E-4 atm-m^3/mol
Environmental transport (Fugacity Level III mass percentages from most likely emission scenario-air)*	Air = 91.8% Water = 5.0% Soil = 3.2% Sediment = <0.1%
Koc*	24.9
Biodegradation	<0.1% after 28 days (OECD Closed Bottle Test) 8-14% after 28 days (CITI Closed Bottle Test)

* Estimated using EPIWIN

5.2.1 Photodegradation

Gas-phase photodegradation of the test material was determined by direct photolysis under static conditions in chambers subjected to artificial light at λ = 300 and 360 nanometers. After 24 hours, 67.8% of the test substance photodegraded (Coulston and Korte, 1987).

Photodegradation with hydroxyl radical sensitizer was estimated using EPIWIN/Aop (v1.90). An overall hydroxyl radical rate constant of 1.7 E-13 cm^3/(molecule*sec) was calculated based on the summation of individual rate constants for each bond fragment in the molecule using the program algorithm. A half-life of 63.6 days was calculated assuming a constant concentration of OH radical and pseudo first order kinetics.

5.2.2 Stability in Water

The stabilities of nitroalkanes in both water and aqueous mineral acids have been determined in a well conducted study (Cundall and Locke, 1968). Nitromethane, nitroethane, 1-nitropropane and 2-nitropropane did not hydrolyze appreciably in neutral water, even at elevated temperatures. The first three (primary) nitroalkanes underwent hydrolysis in aqueous mineral acid solution, and the hydrolysis rate constants were determined (see dossier summary). 2-Nitropropane itself (a secondary nitroalkane) was stable to hydrolysis even in hot mineral acids.

5.2.3 Fugacity

Level III fugacity modeling has been conducted on the test material using the EPIWIN model. Inputs to the program are CAS No. 79-46-9, a melting point of –91.3 ºC, a boiling point of 120ºC, a vapor pressure of 17.32 hPa and a water solubility of 17,400 mg/l. Emission rates

inputted into the program were air: 1000 kg/hr, water: 1000 kg/hr, soil: 1000 kg/hr and sediment: 0 kg/hr. The percent mass balances predicted for this substance in the most likely emission scenario in air, water, soil and sediment are shown in Table 3.

5.2.4 Biodegradation

Two studies were reviewed, summarized, and rated as being acceptable. The critical study (OECD Guide-line 301 D Closed Bottle Test) performed with domestic, non-adapted, activated sludge showed < 0.1% biodegradation of 2-nitropropane after 28 days (Freitag *et al.*, 1990). An additional closed bottle study performed by the Chemicals Inspection and Testing Institute of Japan with sludge showed 8-14 % biodegradation after 28 days (CITI, 1992). Taken together, the results suggest that the material is not readily biodegradable, but is capable of being biodegraded to some extent under certain test conditions.

5.2.5 Summary/Test Plan for Environmental Fate Parameters

Experimental or modeled data are available for all environmental fate endpoints. Adequate studies have been performed to address water stability and biodegradation. Estimated values are available for the hydroxyl radical induced photolysis rate constant and atmospheric half-life, Henry's Law Constant, and Fugacity Level III environmental transport parameters. No further testing is planned for these endpoints.

5.3 Ecotoxicity

5.3.1 Acute Toxicity to Fish

Results of a 48-hour OECD Guideline 203 study conducted in Brachydanio rerio (zebrafish) indicate a no effect concentration (NOEC) of 500 mg/l and a lethal concentration in 50% of the fish (LC50 value) of 620 mg/l (Coulston and Corte, 1987; Freitag *et al.*, 1990). Although few details were provided, the study appears to be valid since it was performed according to an established guideline in a closed system (which would limit volatization), and test material concentrations were analytically confirmed. The study was given a reliability rating of 2 (valid with restrictions) since results were not detailed and purity of the test material was not listed. An additional study that was not performed in a closed system indicated that the 96-hour LC50 value for Pimephales promelas (fathead minnow) was > 612.5 mg/l (Curtis and Ward, 1981). This study is not considered to be as reliable as the OECD Guideline 203 study since the LC50 value appears to have been calculated using nominal concentrations and test material may have escaped due to volatization.

5.3.2 Acute Toxicity to Aquatic Invertebrates

An OECD Guideline 202 test performed with Daphnia magna indicates that the 24-hour EC50 value in this species is 290 mg/l (Coulston and Corte, 1987; Freitag *et al.*, 1990). Although closed systems do not appear to have been used, concentrations were analytically confirmed. The study was given a reliability rating of 2 (valid with restrictions) due to a lack of documentation.

5.3.3 Acute Toxicity to Aquatic Plants

The 72-hour EC50 value for Scenedesmus subspicatus obtained from an OECD Guideline 201 study was 1088 mg/l (Coulston and Corte, 1987; Freitag *et al.*, 1990). For this test, the index of toxicity was inhibition of growth rate. The study was given a reliability rating of 2 (valid with restrictions) since the report was not detailed and concentrations of test material were not analytically confirmed. However, since this study was performed in a closed system, it is likely that escape of test material through volatization was minimized. Therefore, the results are considered to be valid.

5.3.4 Summary/Test Plan for Ecotoxicity

Results of adequate studies in zebrafish, fathead minnows and Daphnia magna show that 2-nitropropane is of low toxicity to these species according to the USEPA, Hazard Evaluation Division, Office of Pesticide Programs. Scenedesmus subspicatus algae are less sensitive to 2-nitropropane than fish or Daphnia. No additional testing is planned.

Results of ECOSAR modeling showed EC/LC_{50} values for fish, Daphnia and algae that were 1.2 times larger, 2-3 times larger, and 2-3 times smaller than experimental values for the respective species. Therefore, these analyses were not considered to be reliable and were not summarized.

5.4 Human Health Data

5.4.1 Acute Mammalian Toxicity

This endpoint is filled by sufficient inhalation studies in rats and mice (Baldwin and Williams, 1977; Dequidt *et al.*, 1973), and one dermal toxicity study in rabbits (Wilbur and Parekh, 1982). The oral toxicity study that was available for review in rats and mice was given a reliability rating of 4 (not assignable) due to lack of information, and will not be discussed.

The inhalation 6-hour LC_{50} values (lethal concentrations in 50% of the animals) obtained from the Baldwin and Williams study were 400 and 720 ppm in male and female rats, 558 and 560 ppm in male and female mice. Clinical signs observed in this study were slight depression, hyperventilation and cyanosis. This study is considered to be the critical study for the endpoint, and was given a reliability rating of 1 (valid without restriction). In an additional inhalation study, the 4 hour LC_{50} value for inhalation of 2-nitropropane of unknown purity was < 14,700 ppm (the LC_{100}). Inhalation of 760 ppm for 8 hours/day over a period of 2 days also produced lethality in all rats tested. Rat exposed to 80 ppm, 8 hours/day for 5 days survived. The methemoglobin concentration in blood of the rat exposed to 14,700 ppm was 84%. No methemoglobin was found in the blood of animals exposed to 80 ppm.

Dermal exposure to 2,000 mg/kg 2-nitropropane did not cause death, clinical signs of toxicity or skin irritation in rabbits.

5.4.2 Repeated Dose Mammalian Toxicity

The potential for significant human exposure to 2-nitropropane is strictly limited; however,

repeated dose inhalation toxicity data in experimental animals are available. The results of previously conducted studies are summarized in Table 4.

The effect of repeated, subchronic (6 month) exposure to 27 or 207 ppm 2-nitropropane was studied in male rats and rabbits. In both studies, the NOAEL was 27 ppm. The investigators did not consider the hematological changes in rats or rabbits exposed to 27 or 207 ppm to be related to treatment. Possible reasons for this conclusion are that the changes observed were generally sporadic and not dose-dependent. Repeated exposure to 207 ppm was associated with pulmonary lesions and edema, and hepatocellular hypertrophy, hyperplasia, and carcinoma in male rats, and transient pulmonary toxicity and changes in liver enzymes (but no histologic evidence of liver toxicity) in male rabbits.

The effect of inhalation of lower concentrations (100 and 25 ppm) for longer amounts of time (18 and 22 month, respectively) was tested in male and female rats. Chronic exposure of 100 ppm 2-nitropropane was associated with biochemical, gross and histologic evidence of irreversible toxicity to the liver and hepatocellular carcinoma in male rats. Female rats did not exhibit increases in liver neoplasms, but had increased incidences of hepatic masses and nodules with hyperplasia and vacuolar degeneration. Renal calcification also was noted in more exposed animals than controls. Investigators conducting the study with 25 ppm did not consider any of the findings in the study as being adverse, and consequently established a NOAEL of 25 ppm. However, at 25 ppm, there was a small increase in the incidences of focal vacuolization and liver congestion in exposed males. Since the liver is the organ targeted by higher concentrations, any effects on the liver at lower doses should be considered to be related to treatment. Therefore, the NOAEL is < 25 ppm.

Table 4. Repeated Dose Toxicity of 2-nitropropane

Species/ Exposure	Dose[a] (deaths)	Gross Changes	Histopathological Changes	Clin. Chem/Hemat. Changes
SD male rat, 6 months, inhalation (Huntingdon Research Center, 1977; Lewis *et al.*, 1977)	27 [b] 207 [c]	↑ wet/dry lung weight ↑ lung, wet/dry lung, liver weight	none lungs, liver	↑ and ↓ in Hct and rbc, ↑ Hb, MetHb ↓ rbc, Hb, ptt, ↑ and ↓ rbc, ↑ MetHb, GPT, thyroxin
SD rat, 18 months, inhalation (Coulston *et al.*, 1985; Griffin and Coulston, 1983)	100 [c]	↓ bw, ↑ liver weight	liver (neoplastic), kidney (non-neoplastic)	↑ GPT
SD rat, 22 months, inhalation (Griffin *et al.*, 1980, 1981)	25 [c]	↑ bw, liver weight	liver (non-neoplastic)	↑ Hb, Hct, rbc, wbc
NZ White male rabbit, 6 months, inhalation (Huntingdon Research Center, 1977; Lewis *et al.*, 1977)	27 [b] 207 [c]	none none	none lungs (1 month only)	none ↑ OCT

Hct = hematocrit, Hb = hemoglobin, rbc = red blood cells, wbc = white blood cells, MetHb = methemoglobin, ptt = prothrombin time; GPT= glutamic-pyruvic transaminase; OCT = ornithine carbamyl transferase [a] Dose is in ppm; [b] No effect level assigned to study; [c] Low effect level assigned to study

The carcinogenic effect of 2-nitropropane on the liver is discussed in more detail in Section 5.4.2.3.

5.4.3 Genetic Toxicity

5.4.3.1 Mutagenicity

2-Nitropropane has been tested for mutagenicity in adequate studies employing *S. typhimurium* strains TA92, TA98, TA100, TA102 and TA1537 (Hite and Skeggs, 1979; Conaway *et al.*, 1991). The material tested positive in all strains in the presence or absence of S-9 (with the exception of TA102 in the absence of S-9).

5.4.3.2 Chromosomal aberration

The effect of 2-nitropropane on the incidences of micronuclei in rat liver and bone marrow cells was studied in conjunction with 1-nitropropane (George *et al.*, 1989). In this test, there was no significant difference in the numbers of micronucleated polychromatic erythrocytes (PCE) in

bone marrow cells from rats exposed by gavage to concentrations up to 300 mg/kg. In contrast, the numbers of micronucleated PCE in hepatocytes isolated from animals treated by gavage with 25 or 50 mg/kg 2-nitropropane were increased with respect to control. The elevated micronucleus frequencies in hepatocytes of treated animals were accompanied by decreases in mitotic index, suggesting that the result was not due to increased proliferation (and therefore, was a true positive). This study was given a reliability rating of 1 (valid without restriction) and is considered to be the critical study for the endpoint.

5.4.4 Reproductive and Developmental Toxicity

Fertility studies with 2-nitropropane have not been conducted; however, repeated dose toxicity studies have included evaluations of gonads of treated animals and an OECD TG 422 screening repeated dose/reproductive/developmental screening toxicity study on a close analogue, 1-nitropropane, have been conducted (Carney *et al*., 2003).

Results of one of the repeated dose toxicity studies previously described in Section 5.4.2 indicate that repeated inhalation of 25 ppm 2-nitropropane for 22 up to 22 months had no effect on the histopathology of the prostate, seminal vesicle, testis, uterus, or ovary of rats (Griffin *et al*., 1980, 1981).

In a study designed to assess the effect of 2-nitropropane on dominant lethal mutations, male rats were exposed repeatedly to a toxic concentration of 2-nitropropane (200 ppm) by inhalation five days prior to mating, and were mated weekly for a total of 9 weeks (McGregor, 1981). There was no effect of treatment on any parameter measured (pregnancy rate, numbers of corpora lutea or total implantations per pregnancy, frequencies of live implantations or live implantations and late deaths, frequency of early death, or on the numbers of animals with one or more or two or more early deaths).

An OECD TG 422 repeated dose/reproductive/developmental toxicity screening study has been conducted on a close analogue, 1-nitropropane (Carney *et al*., 2003). Female rats were exposed 6 h/day to up to 100 ppm 1-nitropropane vapors from 2 weeks pre-mating through mating to gestation day 19. Males were exposed from 2-weeks pre-mating through mating. No treatment-related effects upon reproductive indicies, time to mating, gestation length, post-implantation loss, pup survival, pup sex ratio or gonadal tissues were observed.

Finally, an additional study designed to assess the genotoxcity of 2-nitropropane, inhalation of 200 ppm nitropropane for 5 days had no effect on the frequency of abnormal sperm in mice (McGregor, 1981). This study was given a reliability rating of 4 (not assignable), since the positive control material ethylmethanesulphonate also had no effect on sperm.

The only developmental toxicity study located on 2-nitropropane was one in which the effect of daily i.p. administration of 170 mg/kg 2-nitropropane during gestation days 1-15 on development of rats was assessed (Harris *et al.*, 1979; Hardin *et al.*, 1981). There was no evidence of teratogenicity in offspring from treated dams and no treatment-related changes in organ weights or histology of maternal tissues. However, the authors stated that retarded heart development (1-2 days) was observed in 9 out of 10 litters and 30 to 86 percent of the pups per litter. This study was given a reliability rating of 2 (valid with restrictions), since evidence supporting the

conclusion of "delayed heart development" was not presented, standard assessments of maternal toxicity such as maternal weight, feed consumption and clinical signs were not measured, and the route of exposure was not relevant for humans.

As noted, an OECD TG 422 repeated dose/reproductive/developmental toxicity screening study has been conducted on a close analogue, 1-nitropropane (Carney *et al*., 2003). Exposure of female rats 6 h/day to up to 100 ppm 1-nitropropane vapors from 2 weeks pre-mating through mating to gestation day 19 did not result in any evidence of a teratogenic response.

5.4.5 Additional Data

5.4.5.1 Skin and Eye Irritation

Adequate studies in rabbits show that undiluted 2-nitropropane is not irritating to skin and slightly irritating to eyes (Parekh and Wilbur, 1982; Machle, *et al*., 1940; Reagan, 1989; Barnes, 1974).

5.4.5.2 Sensitization

Results of an adequate study in guinea pigs indicate that 2-nitropropane is not a sensitizer (Parekh, 1982).

5.4.5.3 Carcinogenicity

The results of repeated dose toxicity studies described in Section 5.4.2 indicate that 2-nitropropane is carcinogenic in male rats. Repeated inhalation exposure of rats to 100 ppm for a period up to 18 months had no adverse effect on the total numbers of tumors in males and females, the total numbers of females or males with tumors, the types of tumors in females, or the types of benign tumors in males. However, the types of malignant tumors in exposed males were different from controls. Whereas the most common malignant tumors in control males were fibrosarcoma of the skin and subcutis (N = 1), the most common malignant tumor in exposed males was hepatocellular carcinoma (N=7). Rapidly growing, multiple hepatocellular carcinomas and numerous neoplastic nodules were present in the livers of all 10 male rats exposed to 207 ppm 2-nitropropane for 6 months. Long term inhalation of 25 or 27 ppm had no effect on the incidences of tumors in male (or female) rats, and exposure of rabbits to concentrations that are carcinogenic in rats did not have any effect on the incidences of any tumors.

5.4.5.4 Epidemiology

A retrospective mortality study was conducted to determine if there were any unusual cancer or other disease mortality patterns among Sterlington, Louisiana workers, either before or after the beginning of production of 2-nitropropane (Miller and Temple, 1979; Bolender, 1983). The initial study included 1,815 employees that had worked at the plant from 1946 to 1977, and an updated study included 1,915 employees that were employed from 1946 to 1981. The relationship of race, sex, county of residence, work activity (direct, indirect or no exposure to 2-nitropropane) and years of employment (both prior to and after the start of 2-nitropropane

production) to the type of death coded according to the eighth revision of the International Classification of Diseases was examined. The results indicated that there were no clear trends between years of direct or indirect exposure to 2-nitropropane, and the numbers (or types) of deaths. In the first study, the only disease-related type of death that was increased was "other lymphatic cancer" in white or black, male employees. In the follow-up study, the incidence of "other lymphatic cancer" was not increased in white males. In both studies, the increase in "other lymphatic cancer" in black males was due to bleeding gastric ulcer-lymphosarcoma in one individual and mycosis fungoides in another. Therefore, they appeared to be unrelated and not due to employment. No deaths resulted from cancer of liver (malignant neoplasm, or ICD code 155), which includes hepatocellular carcinoma. Also, no cases of benign neoplasms (tumors) of the liver (ICD code 230.5) were reported.

5.4.6 Summary/Test Plan for Mammalian Toxicity

Adequate acute inhalation toxicity studies have been conducted for 2-nitropropane. Results of these studies show that the NOAEL for inhalation is 400-720 ppm in rats and mice. The material is not acutely toxic by the dermal route and is only slightly irritating to skin. It does not cause irritation to the eyes and is not a sensitizer.

Results of studies that have been performed on 2-nitropropane or a close analogue, 1-nitropropane, are adequate to fulfill repeated dose and reproductive toxicity endpoints. Results of adequate repeated dose inhalation studies show that repeated, long-term inhalation exposure to concentrations ≥ 100 ppm is associated with non-neoplastic and neoplastic changes in the liver of male rats. Female rats exposed to 100 ppm for 22 months did not exhibit increases in liver neoplasms, but had increased incidences of hepatic masses and nodules with hyperplasia and vacuolar degeneration. Long-term exposure to 25-27 ppm caused small increases in the incidences of focal vacuolization and liver congestion in male rats, but did not have any effect on female rats or rabbits. Although a mating study on 2-nitropropane has not been performed, the 6-month repeated dose toxicity test with 25 ppm fills the reproductive toxicity endpoint since reproductive organ toxicity was assessed as well as results of an OECD TG 422 repeated dose/reproductive/developmental toxicity screening study on a close analogue, 1-nitropropane. There also was no evidence of an increase in dominant lethality or sperm abnormality in rats or mice exposed to 2-nitropropane. Daily i.p. administration of 170 mg/kg 2-nitropropane during gestation days 1-15 had no effect on the incidences of malformations, but was associated with delayed heart development. Exposure of rats to up to 100 ppm 1-nitropropane, a close analogue of 2-nitropropane, as part of an OECD TG 422 repeated dose/reproductive/developmental toxicity screening study revealed no evidence of potential teratogenicity. The repeated dose, reproductive and developmental toxicity of 2-nitropropane is adequately characterized by these tests. No additional testing for these endpoints is planned.

Adequate studies show that 2-nitropropane is mutagenic to bacteria and causes an increase in micronucleated liver cells. There is clear evidence of liver carcinogenicity in male rats repeatedly exposed to concentrations ≥100 ppm 2-nitropropane by inhalation. No additional genetic toxicity testing is planned.

6. Summary

In summary, valid data are available for 2-nitropropane to satisfy all physical/chemistry, environmental, ecotoxicity endpoints, and mammalian toxicity endpoints.

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